REMARKS

Claims 1, 6-8, 10-13, 15-20, 22-24, 46, 48 and 52-56 stand provisionally rejected on the ground of obviousness type double patenting for purportedly being unpatentable over claims 1, 3-7, 11-13, 28 and 29 of copending application no. 11/520,640.

MPEP § 804(I)(B) indicates that a provisional OTDP rejection over another application should be made unless the provisional double patenting rejection is the only rejection remaining in at least one of the applications. In the present instance, the other application 11/540,640 was filed after the present application. Because the claims in the present application are otherwise allowable as discussed below, the Examiner should withdraw the provisional OTDP rejection in the present case and allow it to issue.

Claims 1, 6-8, 10-13, 15-20, 22-24, 46, 48 and 52-56 stand rejected under 35 U.S.C. 102(a)/(e) as being anticipated by US Publ. NO. 2007/0025989 (102(e)) or WO/2003/072040. In view of the following remarks Applicants request that the Examiner reconsider and withdraw the rejection of the claims.

Applicants note that US Publ. No. 2007/0025989 is application no. 11/540,640 cited in the obviousness double patenting rejection above. The inventors in application no. 11/540,640 and WO/2003/072040 were under an obligation to assign the invention to the Assignee of the present application and as such the disclosure of US Publ. No. 2007/0025989 is not work by "another." Thus US Publ. NO. 2007/0025989 and WO/2003/072040 is not prior art to this application under 35 U.S.C. 102(a)/(e). Applicants request that the Examiner reconsider and withdraw the rejection of the claims.

Claims 1, 6-8, 10-13, 15-16, 46, 48 and 52-56 stand rejected under 35 U.S.C. 102(a) as being anticipated by Miller et al. (N Engl J Med (2003 Jan 2)

348:15-23). In view of the following remarks, Applicants request that the Examiner reconsider and withdraw the rejection.

Miller reports the results of a controlled trial of natalizumab for relapsing multiple sclerosis. Miller administers natalizumab or placebo every 28 days for 6 months and states that the subjects had fewer brain lesions and fewer relapses than untreated patients. But Miller indicates that the treated patients were still developing new brain lesions and still displayed relapses and the combined values obtained at month 9 and month 12 showed that the number of new enhancing lesions and scans showing activity were similar in all the groups, those receiving the placebo, 3mg/kg natalizumab or 6mg/kg natalizumab. Thus while the Miller treatment regimen may have slowed an aspect of disease progression, Miller does not teach a method that promoted *remyelination* or *reversal of paralysis*. Therefore, Miller does not teach Applicants' method for promoting remyelination of nerve cells by chronically administering an antibody that binds to alpha-4 beta-1 integrin, e.g., natalizumab, in a remyelinating effective amount weekly or monthly over a period of at least 6 months, or at least one year as recited in claims 18 and 56. As such Miller does not anticipate the invention as claimed.

In view of the foregoing remarks Applicants request that the Examiner reconsider and withdraw the rejection of the claims.

Claims 1, 6-8, 10-13, 15-16, 18-20, 22-24 46, 48, and 52-56 stand rejected under 35 U. S.C. 102(a) for purportedly being anticipated by National Horizon Scanning Centre (July 2002) already of record. In view of the following remarks, and the remarks of record, Applicants request that the Examiner reconsider and withdraw the rejection.

In addition to Applicants' remarks already of record, Applicants note that National Horizon summarizes results that were presented on the Elan Corporation's w ebsite www.elan.com/research/antegren.asp Accessed April 16,

2002 (see National Horizon page 3 after "Effectiveness" reference number 6) and states that patients with relapsing-remitting MS or secondary progressive MS received either iv natalizumab (3mg/kg or 6mg/kg) or placebo every 4 weeks for 6 months. As such the results presented on the Elan Corporation's website and cited in National Horizon is not "work by another" and does not qualify as prior art under 35 U.S.C. 102(a)

The Examiner also cites National Horizons' discussion of the results of Tubridy et al., already of record (see National Horizon page 3 after "Effectiveness" reference number 7.) In particular, National Horizons cites Tubridy's report that the patients received only two iv infusions of natalizumab or placebo 4 weeks apart and then followed for up to 24 weeks with serial MRI and clinical assessment. Tubridy did not disclose chronically administering natalizumab monthly or weekly for at least 6 months, or at least a year as recited in claims 18 and 56 and therefore does not anticipate the invention as currently claimed.

Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 102(a) over National Horizons for purportedly anticipating the claims.

Claims 1, 6-8, 10-13, 15-16, 18, 46, 48 and 52-56 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tubridy et al for the reasons of record. Applicants disagree for the reasons of record and in view of the following remarks.

The Examiner states that Applicant's arguments, including the issue of long-felt need are not found persuasive of the patentability when the claimed invention would flow logically from the teaching of the prior art of record. Applicants disagree. Prior to Applicant's teaching no other treatment, even treatments that reduced inflammation, produced the remyelinating effects obtained by Applicants' method as claimed. Thus one of skill in the art based on

the prior art of record at the time of this invention would not have expected a chronic natalizumab treatment method to promote remyelination.

Tubridy et al. does not suggest the steps of Applicants' method as claimed and in fact teaches away for Applicants' method steps by stating that while there were significant differences at 12 weeks, such was not the case at 24 weeks and that the relatively modest correlations between disability and changes seen on MRI means that any potential new treatment must ultimately be tested in a larger longer term trial. Tubridy states:

> "to obtain adequate serum concentration of Antegren [natalizumab] between monthly infusions and to maintain suppression of MRI activity , a higher dose of Antegren administered chronically will need to be evaluated in future studies. It is possible, however, that repeated dosing with a mAb could lead to anti-idiotype antibodies and if of sufficient magnitudes, a loss of efficacy. Further studies are needed to determine more accurately the magnitude and duration of the effect of Antegren on MRI.

Thus Tubridy et al. is only suggesting further experimentation, not the particular steps of Applicants 's method as claimed and as such fails to render the claimed invention obvious.

Claims 1, 6-8, 10-13, 15-16, 18, 46-48 and 52-56 stand rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over U.S. Patent No. 5,840,299 ("the '299 Patent") in view of Tubridy. In view of the following remarks, and the remarks of record, Applicants request that the Examiner reconsider and withdraw the rejection.

Applicants submit that the '299 Patent and Tubridy in combination fail to suggest the particular steps of Applicants' method or suggest the unexpected benefits produced by Applicants' claimed method.

The '299 Patent does not teach the chronic administration of the antibody over a period of at least 6 months or at least 1 year and is silent regarding

"remyelination of nerve cells" and "reversing paralysis." Furthermore, Tubridy teaches that at 24 weeks after patients received two IV administration of anti-α4 integrin antibody 4 weeks apart there were no significant difference in the number of new active or new enhancing lesions between the groups of treated and control patients. Thus Tubridy only teaches a regimen that may *slow* progression of the disease, but there is no teaching or suggestion of a regimen that would *promote remyelination or reverse paralysis*. Thus one of skill in the art considering the '299 Patent in combination with Tubridy would not expect that the chronic administration of natalizumab over a period of at least 6 months, or at least a year for claims 18 and 56, would promote remyelination and reverse paralysis.

One of skill in the art evaluating the '299 Patent and Tubridy in combination and in the context of the state of the art at the time of filing, and considering that prior to Applicants' invention no treatment regimen had ever produced remyelination or reversal of paralysis, would not have reasonably expected and would be surprised that the chronic administration of a remyelinating amount of an anti-α4 integrin, e.g., natalizumab, would promote remyelination and reversal of paralysis.

The combination of the '299 Patent and Tubridy fail to render the invention as currently claimed obvious and Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 103(a).

Claims 1, 19-20 and 22-24 stand rejected under 35 U.S.C. 103(a) for purportedly being unpatentable over the '299 Patent in view of Tubridy and further in view of US Patent No. 6,753,135. Applicants disagree and in view of the following remarks request that the Examiner reconsider and withdraw the rejection.

The Examiner states that the '135 patent teaches prednisone is a corticosteroid used to treat a wide variety of inflammatory disorders including multiple sclerosis. However, Applicants submit that despite the long history of prednisone use, it is not known to promote remyelination. The '299 Patent and Tubridy et al. do not disclose Applicants' discovery that chronic administration of natalizumab, surprisingly, is useful for promoting remyelination. Therefore at the time of this invention based on the teaching of the cited art one of ordinary skill in the art would not combine prednisone with natalizumab in a method to promote remyelination. As such, the combination of the '299 Patent, Tubridy and the '135 Patent fails to render Applicants' invention as claimed obvious.

Claims 1, 19-20 and 22-24 stand rejected under 35 U.S.C. 103(a) for purportedly being unpatentable over Miller et al. further in view of the '135 Patent. Applicants disagree.

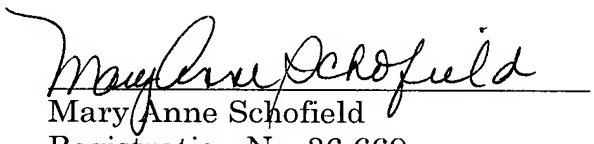
As discussed above, the '135 patent may teach that prednisone is a corticosteroid used to treat a wide variety of inflammatory disorders including multiple sclerosis, but prednisone has never been shown to promote remyelination and as such one of skill in the art would not use prednisone to promote remyelination. Likewise, the Miller et al. fails to teach or suggest Applicants' discovery that their method of chronically administering natalizumab promotes remyelination. Therefore based on the teachings of the cited art, one of ordinary skill in the art would not combine prednisone with natalizumab in a method to promote remyelination. As such, the combination of Miller et al. and the '135 Patent fails to render Applicants' invention as claimed obvious and Applicants request that the Examiner reconsider and withdraw the rejection over Miller et al. further in view of the '135 Patent.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323, Docket No. 103930.B080061.

Respectfully submitted,

March 11, 2010



Mary Anne Schofield
Registration No. 36,669

CROWELL & MORING LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844
MAS:mas